

CLAIMS

1. A monoclonal anti-idiotypic antibody against a human Factor VIII inhibitory antibody, the said inhibitory antibody being directed towards the C2 domain of Factor VIII.
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2. The monoclonal anti-idiotypic antibody according to claim 1, further characterised in having the ability to neutralise by at least 50% the inhibition of FVIII procoagulant activity mediated by inhibitory antibodies against the C2 domain of FVIII.
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3. The monoclonal anti-idiotypic antibody according to claim 1 or 2, which does not interfere with binding of FVIII to Phospholipids and/or vWF.
- 15 4. The monoclonal anti-idiotypic antibody according to any one of claims 1 to 3 wherein the said Factor VIII inhibitory antibody has a variable heavy chain of which the VH domains are encoded by the DP5 VH gene segment derived from the VH1 gene family.
- 20 5. The monoclonal anti-idiotypic antibody according to any one of claims 1 to 4 wherein the Factor VIII inhibitory antibody is BO2C11.
6. The monoclonal anti-idiotypic antibody according to any one of claims 1 to 4 wherein a complementary determining region of the variable heavy and light chains of said antibody has at least 70 % sequence identity to one of amino acid sequences depicted in SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 SEQ ID NO:9 and SEQ ID NO:10.
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7. The monoclonal anti-idiotypic antibody according to any of claims 1 to 5 wherein the variable heavy chain of the said anti-idiotypic antibody is encoded by the nucleotide sequence depicted in SEQ ID NO 1 or a nucleotide sequence having at least 70% sequence identity to SEQ ID NO 1 and/or wherein the variable light chain of the anti-idiotypic antibody is encoded by the nucleotide sequence depicted in SEQ ID NO 3 or a
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nucleotide sequence having at least 70% sequence identity with SEQ ID NO 3.

- 5 8. The monoclonal anti-idiotypic antibody according to any of claims 1 to 6, which is an F(Ab')₂ fragment, an Fab' fragment, an Fab fragment, or a modified version of said fragment.
9. The monoclonal anti-idiotypic antibody according to any of claims 1 to 7,
10 which is a humanized monoclonal anti-idiotypic antibody.
10. The monoclonal anti-idiotypic antibody according to any of claims 1 to 9, which is 14C12 or an antibody derived therefrom.
- 15 11. An isolated and purified peptide having an amino acid sequence selected from SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9 and SEQ ID NO:10 being at least 70 % identical in amino acid sequence to a peptide with an amino acid sequence selected from SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9 and SEQ
20 ID NO:10.
12. A monoclonal cell line expressing a monoclonal anti-idiotypic antibody in accordance with any of claims 1 to 10.
- 25 13. The monoclonal cell line in accordance with claim 12, which is the cell line 14C12 deposited at BCCM with Accession Number LMBP 5878CB.
14. A pharmaceutical composition comprising a monoclonal anti-idiotypic
30 antibody according to any of claims 1 to 10, or an isolated and purified peptide according to claim 12 in admixture with at least one pharmaceutically acceptable carrier.

15. Use of a monoclonal anti-idiotypic antibody according to any one of claims 1 to 10 or an isolated and purified peptide according to claim 12 as a medicine.

5 16. A method of treating patients suffering from the effects of FVIII inhibitory antibodies, said method comprising, administering to said patient a therapeutically effective dose of the pharmaceutical composition according to claim 14.

10 17. A method of treatment or prevention of uncontrolled bleeding in a patient with FVIII inhibitory antibodies, said method comprising administering to said patient a therapeutically effective dose of the pharmaceutical composition according to claim 14.

15 18. The method according to claim 17, which further comprises administering to said patient FVIII.

19. The method of any one of claims 16 to 18, wherein said patient is a haemophiliac.

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20. A method for developing monoclonal anti-idiotypic antibodies for the manufacture of a medicament against FVIII inhibitors, said method comprising immunizing an animal with inhibitory antibodies directed against the C2 domain of factor 8 and screening the immortalized spleen cells of said animal for the production of antibodies which a) neutralise the
25 anti-coagulant activity of FVIII inhibitors for at least 50% and b) do not interact with the binding of FVIII to vWF and phospholipids.

21. The use of the anti-idiotypic antibodies of any one of claims 1 to 10 for the
30 detection or purification of inhibitory FVIII antibodies.